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New Data on RYBREVANT® (amivantamab-vmjw) in Combination with Lazertinib Show Early Activity in Patients with Non-Small Cell Lung Cancer Whose Disease Has Progressed After Both Osimertinib and Platinum-Based Chemotherapy

CHRYSALIS-2 findings presented at ESMO Annual Congress 2021 suggest that RYBREVANT® and lazertinib combination has encouraging anti-tumor activity in this population that has exhausted standard-of-care treatments

September 19, 2021 (RARITAN, N.J.) – The Janssen Pharmaceutical Companies of Johnson & Johnson today announced preliminary results from the Phase 1b CHRYSALIS-2 (NCT04077463) study evaluating RYBREVANT® (amivantamab-vmjw) in combination with lazertinib in the treatment of patients with non-small cell lung cancer (NSCLC) characterized by epidermal growth factor receptor (EGFR) exon 19 deletion or L858R mutations whose disease had progressed after treatment with osimertinib and platinum chemotherapy.[1] While previously reported results have demonstrated durable responses with RYBREVANT® in combination with lazertinib in chemotherapy-naïve patients previously treated with osimertinib, these new data suggest that intervening chemotherapy does not impact activity with the combination.[1] These data were featured for the first time in a mini-oral presentation at the European Society for Medical Oncology (ESMO) Annual Congress 2021 virtual meeting on Sunday, September 19 (Abstract #1193MO).

"Patients with non-small cell lung cancer whose disease has progressed despite receiving standard of care treatments have a tremendous need for additional treatment options," said Catherine A. Shu, M.D., Clinical Director of the Thoracic Medical Oncology Service, Columbia University Herbert Irving Comprehensive Cancer Center, and presenting study investigator.† "We are encouraged by these data showing that the combination of amivantamab and lazertinib elicited antitumor activity, even in a heavily pretreated patient population."

In Cohort A of the CHRYSALIS-2 study, patients with NSCLC with EGFR exon 19 deletion or L858R mutations whose disease had progressed after treatment with osimertinib and platinum chemotherapy received the recommended combination dose of RYBREVANT® at 1050 mg (for patients who weigh <80kg) or 1400 mg (for patients who weigh ≥80 kg) and oral lazertinib at 240 mg.[1] The study also included a heavily pretreated population (n=56), who received platinum-based chemotherapy, osimertinib and other therapies, with no prespecified number or sequence of prior treatment.[1] A protocol amendment created a target population (n=80), which specified progression on osimertinib and platinum-based chemotherapy, in that order.[1]

The efficacy data presented is by investigator-assessed response per Response Evaluation Criteria in Solid Tumors Version 1.1* (RECIST v1.1) in patients that have undergone at least two post-baseline disease assessments.[1,2] Of the 29 efficacy-evaluable patients within the target population (n=80) at a median follow-up of 4.6 months (range; 0.4–9.6), the overall response rate (ORR) was 41 percent (95 percent confidence interval [CI]; 24–61).[1] The clinical benefit rate (CBR), which consisted of complete response, partial response (PR) or stable disease at 11 weeks or longer, was 69 percent (95 percent CI; 49–85).[1] Eight out of 12 patients who responded are ongoing and remain on treatment and five out of 12 patients with stable disease remain on treatment (longest at 6.9+ months).[1]

In the population of heavily pretreated patients (n=56), among the 47 efficacy-evaluable patients at median follow-up of 4.5 months (range; 0.3–9.7), ORR was 21 percent (95 percent CI; 11–36), with a CBR of 51 percent (95 percent CI; 36–66). The median time on treatment was 3.7 months (range; 0.03–9.7) and 10 out of 10 patients who responded remain on treatment. Ten out of 26 patients with stable disease remain on treatment (longest at 9.6+ months).[1] Additionally, responses were observed early with a median time to first confirmed response of 1.5 months (range; 1.3–4.2).[1]

The safety profile with the combination was consistent with previously reported RYBREVANT® and lazertinib results at the recommended combination dose, and no new safety signals were identified.[1] The majority of treatment-emergent adverse events (AEs) were Grade 1-2.[1] Treatment-emergent Grade ≥3 AEs were infusion-related reaction (nine percent), dyspnea (six percent), acneiform dermatitis (four percent), hypoalbuminemia (four percent), paronychia (three percent), increased alanine aminotransferase (three percent), rash (two percent), stomatitis (two percent), asthenia (two percent), nausea (two percent), increased aspartate aminotransferase (two percent), fatigue (two percent), peripheral edema (one percent), thrombocytopenia (one percent), decreased appetite (one percent) and pruritus (one percent).[1]

In May, the U.S. Food and Drug Administration (FDA) approved RYBREVANT®, a fully human bispecific antibody, as the first targeted treatment for patients with NSCLC with EGFR exon 20 insertion mutations.[3] Ongoing studies, including CHRYSALIS-2, are evaluating the potential of RYBREVANT® in combination with lazertinib, a third-generation EGFR tyrosine kinase inhibitor (TKI), across multiple cohorts and for different driver and resistance genetic mutations. Lazertinib was approved earlier this year in South Korea for patients with NSCLC with EFGR mutations and T90M mutations.

"These findings build on previous results showing the potential of RYBREVANT and lazertinib combination therapy in patients with EGFR-mutated non-small cell lung cancer and provide further insights supporting our comprehensive clinical development program in lung cancer," said Craig Tendler, M.D., Vice President, Late Development and Global Medical Affairs, Oncology, Janssen Research & Development, LLC. "As we continue to evaluate RYBREVANT as a monotherapy and in combination with lazertinib, we look forward to continuing to advance science and improve outcomes for people living with advanced NSCLC."

*RECIST (version 1.1) refers to Response Evaluation Criteria in Solid Tumors, which is a standard way to measure how well solid tumors respond to treatment and is based on whether tumors shrink, remain the same or increase in size.[2]

About RYBREVANT®

RYBREVANT® (amivantamab-vmjw) received accelerated approval by the U.S. FDA in May 2021 for the treatment of adult patients with locally advanced or metastatic NSCLC with EGFR exon 20 insertion mutations, as detected by an FDA-approved test, whose disease has progressed on or after platinum-based chemotherapy.[4] Shortly after FDA approval, the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Non-Small Cell Lung Cancer* included amivantamab-vmjw (RYBREVANT®) as a subsequent therapy option with a Category 2A recommendation for patients that have progressed on or after platinum-based chemotherapy with or without immunotherapy and have EGFR exon 20 insertion mutation-positive advanced NSCLC.[5] Janssen has filed regulatory submissions for RYBREVANT® with health authorities in Europe and other markets.

RYBREVANT® is being studied in multiple clinical trials, including the Phase 1 CHRYSALIS (NCT02609776) study to evaluate the safety, pharmacokinetics and preliminary efficacy of RYBREVANT® as a monotherapy and in combination, including with lazertinib, in patients with advanced NSCLC with various EGFR mutations; the Phase 1/1b, CHRYSALIS-2 study (NCT04077463) assessing the combination of RYBREVANT® and lazertinib in patients who have progressed after treatment with osimertinib and chemotherapy; as first-line therapy in untreated advanced EGFR-mutated NSCLC in the Phase 3 MARIPOSA (NCT04487080) study assessing amivantamab in combination with lazertinib; the planned Phase 3 MARIPOSA-2 (NCT04988295) study assessing the efficacy of lazertinib, RYBREVANT® and carboplatin-pemetrexed versus carboplatin-pemetrexed in patients with locally advanced or metastatic EGFR exon 19 deletion or exon 21 L858R substitution NSCLC after osimertinib failure; the Phase 3 PAPILLON (NCT04538664) study assessing RYBREVANT® in combination with carboplatin-pemetrexed versus chemotherapy alone in patients with advanced or metastatic EGFR-mutated NSCLC and exon 20 insertion mutations; and the Phase 1 PALOMA (NCT04606381) study assessing the feasibility of subcutaneous (SC) administration of RYBREVANT® based on safety and pharmacokinetics and to determine a dose, dose regimen and formulation for RYBREVANT® SC delivery.[6,7,8,9,10,11]

*Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Non-Small Cell Lung Cancer V.5.2021. © National Comprehensive Cancer Network, Inc. 2021. All rights reserved. Accessed June 15, 2021. To view the most recent and complete version of the guidelines, visit NCCN.org.

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About Lazertinib

Lazertinib is an oral, third-generation, brain-penetrant, EGFR TKI that targets both the T790M mutation and activating EGFR mutations while sparing wild type-EGFR.[12] Interim safety and efficacy results from the lazertinib Phase 1-2 study were published in *The Lancet Oncology* in 2019. In 2018, Janssen Biotech, Inc. entered into a license and collaboration agreement with Yuhan Corporation for the development of lazertinib.

About the CHRYSALIS-2 Study

CHRYSALIS-2 (NCT04077463) is a Phase 1/1b open-label, multicenter study evaluating the safety, tolerability and preliminary anti-tumor activity of lazertinib, a novel third-generation EGFR TKI, as a monotherapy and in combination with RYBREVANT® in adults with advanced NSCLC.[7] The Phase 1 portion consists of confirming the tolerability of the recommended Phase 2 dose of lazertinib as a monotherapy.[7] The Phase 1b portion consists of assessing the tolerability and identifying the recommended Phase 2 combination dose of lazertinib when combined with RYBREVANT®, and the Phase 1b expansion consists of four cohorts: three to evaluate lazertinib in combination with RYBREVANT® and one to assess two potential biomarker strategies to identify probability of tumor response to the combination of lazertinib and RYBREVANT®.[7] Enrollment in Cohort A has completed, and additional enrollment in Cohort B (exon 20 insertion mutations), C (atypical mutations) and D (post-osimertinib, biomarker validation) are ongoing.[7]

About Non-Small Cell Lung Cancer (NSCLC)

Worldwide, lung cancer is one of the most common cancers, and NSCLC makes up 80 to 85 percent of all lung cancers.[13,14] The main subtypes of NSCLC are adenocarcinoma, squamous cell carcinoma and large cell carcinoma.[14] Among the most common driver mutations in NSCLC are alterations in EGFR, which is a receptor tyrosine kinase supporting cell growth and division.[15] Epidermal growth factor receptors mutations are present in 10 to 15 percent[15,16,17,18,19] of people with NSCLC adenocarcinoma and occur in 40 to 50 percent of Asians.[20,21] The five-year survival rate for all people with metastatic NSCLC and EGFR mutations treated with EGFR TKIs is less than 20 percent.[22,23]

RYBREVANT® IMPORTANT SAFETY INFORMATION[4]

WARNINGS AND PRECAUTIONS

Infusion Related Reactions[4]

RYBREVANT® can cause infusion related reactions (IRR); signs and symptoms of IRR include dyspnea, flushing, fever, chills, nausea, chest discomfort, hypotension, and vomiting.

Based on the safety population, IRR occurred in 66% of patients treated with RYBREVANT®. Among patients receiving treatment on Week 1 Day 1, 65% experienced an IRR, while the incidence of IRR was 3.4% with the Day 2 infusion, 0.4% with the Week 2 infusion, and cumulatively 1.1% with subsequent infusions. Of the reported IRRs, 97% were Grade 1-2, 2.2% were Grade 3, and 0.4% were Grade 4. The median time to onset was 1 hour (range 0.1 to 18 hours) after start of infusion. The incidence of infusion modifications due to IRR was 62% and 1.3% of patients permanently discontinued RYBREVANT® due to IRR.

Premedicate with antihistamines, antipyretics, and glucocorticoids and infuse RYBREVANT® as recommended. Administer RYBREVANT® via a peripheral line on Week 1 and Week 2. Monitor patients for any signs and symptoms of infusion reactions during RYBREVANT® infusion in a setting where cardiopulmonary resuscitation medication and equipment are available. Interrupt infusion if IRR is suspected. Reduce the infusion rate or permanently discontinue RYBREVANT® based on severity.

Interstitial Lung Disease/Pneumonitis[4]

RYBREVANT® can cause interstitial lung disease (ILD)/pneumonitis. Based on the safety population, ILD/pneumonitis occurred in 3.3% of patients treated with RYBREVANT®, with 0.7% of patients experiencing Grade 3 ILD/pneumonitis. Three patients (1%) discontinued RYBREVANT® due to ILD/pneumonitis.

Monitor patients for new or worsening symptoms indicative of ILD/pneumonitis (e.g., dyspnea, cough, fever). Immediately withhold RYBREVANT® in patients with suspected ILD/pneumonitis and permanently discontinue if ILD/pneumonitis is confirmed.

Dermatologic Adverse Reactions[4]

RYBREVANT® can cause rash (including dermatitis acneiform), pruritus and dry skin. Based on the safety population, rash occurred in 74% of patients treated with RYBREVANT®, including Grade 3 rash in 3.3% of patients. The median time to onset of rash was 14 days (range: 1 to 276 days). Rash leading to dose reduction occurred in 5% of patients, and RYBREVANT® was permanently discontinued due to rash in 0.7% of patients.

Toxic epidermal necrolysis occurred in one patient (0.3%) treated with RYBREVANT®.

Instruct patients to limit sun exposure during and for 2 months after treatment with RYBREVANT®. Advise patients to wear protective clothing and use broad spectrum UVA/UVB sunscreen. Alcohol free emollient cream is recommended for dry skin.

If skin reactions develop, start topical corticosteroids and topical and/or oral antibiotics. For Grade 3 reactions, add oral steroids and consider dermatologic consultation. Promptly refer patients presenting with severe rash, atypical appearance or distribution, or lack of improvement within 2 weeks to a dermatologist. Withhold, dose reduce or permanently discontinue RYBREVANT® based on severity.

Ocular Toxicity[4]

RYBREVANT® can cause ocular toxicity including keratitis, dry eye symptoms, conjunctival redness, blurred vision, visual impairment, ocular itching, and uveitis. Based on the safety population, keratitis occurred in 0.7% and uveitis occurred in 0.3% of patients treated with RYBREVANT®. All events were Grade 1-2. Promptly refer patients presenting with eye symptoms to an ophthalmologist. Withhold, dose reduce or permanently discontinue RYBREVANT® based on severity.

Embryo Fetal Toxicity[4]

Based on its mechanism of action and findings from animal models, RYBREVANT® can cause fetal harm when administered to a pregnant woman. Advise females of reproductive potential of the potential risk to the fetus. Advise female patients of reproductive potential to use effective contraception during treatment and for 3 months after the final dose of RYBREVANT®.

Adverse Reactions[4]

The most common adverse reactions (≥20%) were rash, IRR, paronychia, musculoskeletal pain, dyspnea, nausea, fatigue, edema, stomatitis, cough, constipation, and vomiting. The most common Grade 3 or 4 laboratory abnormalities (≥2%) were decreased lymphocytes, decreased albumin, decreased phosphate, decreased potassium, increased alkaline phosphatase, increased glucose, increased gamma-glutamyl transferase, and decreased sodium.

Please read full Prescribing Information for RYBREVANT®.

About the Janssen Pharmaceutical Companies of Johnson & Johnson

At Janssen, we're creating a future where disease is a thing of the past. We're the Pharmaceutical Companies of Johnson & Johnson, working tirelessly to make that future a reality for patients everywhere by fighting sickness with science, improving access with ingenuity and healing hopelessness with heart. We focus on areas of medicine where we can make the biggest difference: Cardiovascular & Metabolism, Immunology, Infectious Diseases & Vaccines, Neuroscience, Oncology and Pulmonary Hypertension.

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†Dr. Shu has been a paid consultant to Janssen; she has not been paid for any media work.

Cautions Concerning Forward-Looking Statements

This press release contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995 regarding RYBREVANT® (amivantamab-vmjw) and lazertinib. The reader is cautioned not to rely on these forward-looking statements. These statements are based on current expectations of future events. If underlying assumptions prove inaccurate or known or unknown risks or uncertainties materialize, actual results could vary materially from the expectations and projections of Janssen Research & Development, LLC, Janssen Biotech, Inc., any of the other Janssen Pharmaceutical companies, and/or Johnson & Johnson. Risks and uncertainties include, but are not limited to: challenges and uncertainties inherent in product research and development, including the uncertainty of clinical success and of obtaining regulatory approvals; uncertainty of commercial success; manufacturing difficulties and delays; competition, including technological advances, new products and patents attained by competitors; challenges to patents; product efficacy or safety concerns resulting in product recalls or regulatory action; changes in behavior and spending patterns of purchasers of health care products and services; changes to applicable

laws and regulations, including global health care reforms; and trends toward health care cost containment. A further list and descriptions of these risks, uncertainties and other factors can be found in Johnson & Johnson's Annual Report on Form 10-K for the fiscal year ended January 3, 2021, including in the sections captioned "Cautionary Note Regarding Forward-Looking Statements" and "Item 1A. Risk Factors," and in the company's most recently filed Quarterly Report on Form 10-Q, and the company's subsequent filings with the Securities and Exchange Commission. Copies of these filings are available online at www.sec.gov, www.jnj.com or on request from Johnson & Johnson. None of the Janssen Pharmaceutical Companies nor Johnson & Johnson undertakes to update any forward-looking statement as a result of new information or future events or developments.

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